UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/404,010	09/23/99	LUO	A-68294/DJB/

EXAMINER: Y

HM22/0214
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ART UNIT	PAPER NUMBER
1646	13

DATE MAILED: 02/14/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/404,010	LUO ET AL.	
	Examiner	Art Unit	
	Janet L Andres	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *11-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-10, in paper no. 12, filed January 4, 2001, is acknowledged. Claims 1-23 are pending in this application. Claims 11-23 are withdrawn from consideration as being drawn to a non-elected invention. The restriction requirement is made FINAL.

Information Disclosure Statement

2. The information disclosure statement filed on July 18, 2000, in paper no. 6 has been fully considered.

Specification

3. The disclosure is objected to because of the following informalities: There are several references on p. 8 to "the Figure". It is not clear which figure is intended.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1,2, and 6-10 are rejected under 35 U.S.C. 102(a) as being anticipated by WO 9905175-A, February, 1999. WO 9905175-A teaches a sequence (SEQ ID NO:3) of overall 41.2% homology to the instant SEQ ID NO:1. This sequence contains a region that an exact

match to position 1359-1859 of SEQ ID NO:1 and also contains a region that has three mismatches with positions 2200-2619. Thus the sequence taught by WO 9905175 would be identified by stringent hybridization, and is encompassed by the claims 1, 2, and 6-10.

6. Claims 1, 2, and 6-10 are further rejected under 35 U.S.C. 102(b) as being anticipated by Myers, June, 1998, GenBank Accession No. G38718. Myers teaches a sequence with 4 mismatches to positions 171-567 of SEQ ID NO:1, which would thus also be identified by hybridization.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. These claims are drawn to nucleic acids encoding for a protein that interacts with TRAF4. Thus, as applicant states, this protein could be used to affect cell division, either in treatment of cancer or to promote proliferation, for example in wound healing. However, the specification as written is not enabling for any of these possible utilities.

" [T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use **the full scope** of the claimed invention without 'undue experimentation.' " In re Wright , 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); see also Amgen Inc. v. Chugai Pharms. Co. , 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); In re Fisher , 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (" **[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.").** Whether making and using the invention would have required undue experimentation, and thus whether the disclosure is enabling, is a legal

conclusion based upon several underlying factual inquiries. See In re Wands , 858 F.2d 731, 735, 736-37, 8 USPQ2d 1400, 1402, 1404 (Fed. Cir. 1988). [emphasis added]

Genentech Inc. v. Novo Nordisk A/S, 42 USPQ2d 1001 (CA FC 1997)

The factors to be considered have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex Parte Forman,* (230 USPQ 546 (Bd Pat. App. & Int. 1986)); *In re Wands,* 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

In the instant disclosure, applicant has provided no teachings as to how the claimed polynucleotides could be used to affect cell division. What is shown is that the encoded protein interacts with TRAF4. Little, however, is known about the role of TRAF-4 in cell division. The receptor with which it associates is not known; unlike other TRAFs, it does not associate with CD-40 (Pullen et al., J. Biol. Chem. 1999, vol. 274, pages 14246-14254) or many other TNF-R-related receptors. While it has been shown to bind LTβR and, weakly, p75-NGF, Krajewska et al. (Am. J. Pathol., 1998, vol 152, pages 1549-1561) teaches that the significance of these interactions are unknown (p. 1559). Further, although Krajewska et al. teaches downregulation of TRAF-4 in tumor cells, others teach upregulation (Tomasetto et al., Am. J. Pathol., 1998, vol. 153, page 2007). Further, controversy exists as to the sub-cellular localization of TRAF-4 (Krajewski et al., Am. J. Pathol., 1998, vol. 153, p. 2008). Thus, since the prior art does not teach the role of TRAF-4 in cell division, the instant teaching that an encoded protein associates with it does not enable a function for the protein, and thus for the encoding nucleic acid. Since one of skill in the art would not know the role of TRAF-4 in cancer or in normal cell division,

such an artisan would not know, without further guidance, how to use a protein that interacts with it.

The instant specification further teaches that the claimed nucleic acid encodes a protein with a kinase domain and homology to MAP kinase and CDK families (p. 5). However, while these teachings might indicate to one of skill that the protein is involved in cell cycling, they do not provide the guidance necessary to allow one of skill to use the protein and thus the encoding nucleic acid. MAP kinases and CDKs have diverse functions (Cook et al., Biochem. Soc. Trans. 2000, vol 28, pages 233-240). MAP kinase-induced pathways can inactivate CDKs (Fig. 1, p. 234); further, the role of MAP kinase itself depends on the duration and magnitude of activation (p. 236). Thus, without further information, the disclosed homology to these kinases would not allow one of skill to predictably use the claimed invention to affect cell division.

The guidance in the specification, therefore, is not sufficient for one of skill to predictably use the claimed invention to affect cancer or such processes as wound healing. Without the ability to predict how the nucleic acid could be used, it would require undue experimentation for one of skill in the art to use the invention. Thus, since the specification is not enabling for any use of the instant polynucleotide, applicant has not set forth a process of using the claimed invention in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains to make and use the same.

9. Claims 1, 4, and 6-10 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are drawn to

nucleic acids encoding a "cell cycle protein" with homology to the disclosed sequence. Applicant has described a TRAF4-associated protein, but the description of this one protein does not adequately describe the scope of the claimed genus, which encompasses all "cell cycle proteins" with the required sequence homology. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly&Co.*, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The specification discloses isolated an cDNA sequence and the translated amino acid sequence. There is no description of the required structural and functional features of related "cell cycle proteins", or of the conserved regions that would be critical for these features. Since these features are not disclosed, there is no way to determine what variations could be tolerated without altering them, and thus what homologues would posses the desired characteristics of a "cell cycle protein". Further, the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify the polynucleotides: no set of characteristics defining a "cell-cycle protein" is understood in the art. Therefore, applicant has not disclosed sufficient species or common structural features such that one skilled in the art would conclude that applicant was in possession of the claimed genus homologues of the disclosed polynucleotide that would encode a "cell cycle protein".

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1, 2, and 6-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims are drawn to molecules hybridizing under high-stringency conditions. The specification (pages 9-10) teaches only that stringency typically occurs anywhere from 5 to 25 degrees below the Tm of the hybridizing DNA which encompasses any size fragment. Nowhere is a specific set of "stringent" conditions given. Since conditions such as DNA molecule size, ionic strength, presence of formamide, time and molecular complexity combine with the degree of nucleotide complementarity to determine the degree of hybridization, predictability of sequences which possess hybridization activity requires knowledge of what conditions, may be modified, to what degree. A nucleotide variant encoding a TRAF4-binding polypeptide which retains binding activity and functional characteristics and is 85% homologous to a specific sequence will require different hybridization conditions from a 10 or 12mer oligonucleotide being used as a probe. Thus the term "stringent hybridization conditions" denotes specific conditions in various situations and cannot be applied, generally, to all DNA sequences as now claimed.

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet Andres, Ph.D., whose telephone number is (703) 305-0557. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564. The fax phone number for this group is (703) 305-3014 or (703) 308-4242.

Communications via internet mail regarding this application, other than those under U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to **[yvonne.eyler@uspto.gov]**.

All Internet email communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Janet Andres, Ph.D.
February 12, 2001

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